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The effects of socioeconomic status on stroke risk and outcomes

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Abstract

The latest international evidence on socio-economic status and stroke shows that stroke not only disproportionately affects low- and middle-income countries, but also socio-economically deprived populations within countries of all income categories. These disparities are found at every stage: from stroke prevention through acute care and rehabilitation, to long-term outcomes. Increased average levels of 'traditional' risk factors (hypertension, hyperlipidaemia, excess alcohol intake, smoking, obesity, sedentary lifestyle) in populations with lower SES appears to explain around half of the effect. In many countries there is evidence that people with lower SES are less likely to receive good quality acute hospital and rehabilitation care. For practice, better implementation of well-established treatments: traditional risk factor treatment and equity of access to high quality acute stroke care and rehabilitation seems likely to reduce inequality substantially. Overcoming barriers and adapting evidence-based interventions to different countries and healthcare settings remains a research priority.

Introduction

Our group's 2006 review summarised the evidence on the disproportionate effect of stroke on people who are socio-economically disadvantaged, in terms of increased incidence and severity, and poor outcome.[1] Since this review was published, several long-running stroke registers and national audits have published large-scale analyses examining the strength and possible mechanisms of the link between socio-economic status (SES) and stroke.

In this update, we present a systematic overview of these developments and discuss the uncertainties which remain, particularly around how best to measure SES, the methodological difficulties in proving a mechanism of the link, and whether intervention can reduce these health inequalities.

Concepts and definitions

Defining SES is complex; the term is typically used to describe a composite measure of a person's income, education, employment, and social status (Figure 1).[2]

In practice, researchers use a large range of measures of SES (see Table 1 below). The measure chosen is often influenced by available data or other idiosyncratic characteristics of the study setting. For example, studies conducted in countries with predominantly private healthcare systems, such as South Korea and the US, have used possession of health insurance as an indicator.[3,4] Many studies from the UK, where last occupation is collected routinely on the registration of death, classify the social status of occupations as a proxy for socio-economic status.[5]

Studies from many countries have used *area-based* measures, which provide an average SES score for small geographic areas, taking into account factors such as average unemployment levels, and average income; the make up of such scores are typically idiosyncratic to individual countries, and depend on the availability of data from national censuses and other sources.[6] The UK has a number of *deprivation indexes* (including the Index of Multiple Deprivation [IMD][7], and the Carstairs score[8]), originally designed to help the allocate public resources to areas most in need; these have been widely used in SES research in the UK;[6] related scores are now used in other countries.[9,10]

Although the measures in Table 1 all broadly measure SES, these important differences mean it is often not possible to make direct comparisons between data from different countries.

	Measures	**Countries where used**	**Advantages**	**Disadvantages**
Education	Highest educational level attained Years in full-time education	Japan, US, Netherlands, UK, Denmark, Australia	Tends to be set in early life (and therefore not reduced by ill-health later in life) Easily obtained	Specific to individual countries, cultures, and education systems
Occupation	Classifications of social status of occupations (e.g. Registrar General Great Britain social classes I–V[5], and the United States Standard Occupational Classification[11])	Japan, UK, Sweden, Netherlands, Australia	Associated with social status, income, and education	Does not account for those who don't work (students, unemployed people) Ill health in adulthood could in principle lead to a lower ranked occupation (i.e. the wrong direction of causation)
Income	For individuals, or household: total income; disposable income	Korea, Sweden, Finland, Denmark, Netherlands	High income facilitates access to education and healthcare, and health promoting environments, activities and goods.	Self reports may be unreliable Low response rates Unequal distribution of income among household members Varies throughout life
Medical	Possession of	Korea, US	Associated with income,	Less relevant in

insurance status	private medical insurance State funding of treatment		and occupation Easily obtainable from routine data collection	countries with universal healthcare
Material ownership/ wealth	Value of assets including housing, cars, monetary assets (investments, pensions, etc.)	Australia	More important to standard of living in retired people; income may be more important in working age people	May be an indicator of lifestyle differences
Area-based measures	Composite of multiple variables, averaged over small geographic areas; individuals typically ranked by quantile	UK, France, Italy, Australia, US, New Zealand, Japan	Easily estimated without need for individual-level data-collection; high data completeness obtained	The Ecological Fallacy: individuals may not be well represented by area data; e.g. an individuals with high SES can live in an area with low average SES Scores vary between studies and countries, meaning direct comparisons often not possible

Table 1. Measures of socio-economic status

Search strategy and selection criteria

A search of MEDLINE was conducted from January 2006 to July 2015 of titles, abstracts and MESH codes using the terms "social class", "income", "education", "poverty", "inequality", "deprivation", "cerebrovascular accident", "cerebrovascular disorders", "cerebral haemorrhage", "subarachnoid haemorrhage", "stroke", and "stroke epidemiology". From the search retrieval, we included prospective cohort studies and retrospective analyses of routine data which reported the association between socio-economic status and stroke incidence, severity, or outcome. We included studies in people with confirmed clinical stroke which assessed associations between SES and any outcome, including mortality, severity, and functional and cognitive impairment. Where good quality systematic reviews with meta-analysis existed, we included these in preference to the source studies. The search retrieval was augmented by hand searching of articles which cite, and were cited by other included studies.

National-level comparisons

The Global Burden of Disease Study systematically reviewed 119 international observational studies, and confirmed that not only does stroke disproportionately affect low- and middle-income countries, but that this discrepancy is worsening.[12] Age-standardised incidence rates in high-income countries have reduced together alongside an increase in low- and middle-income countries (Figure 2).
However, given the increasing and aging populations, the absolute incidence of stroke continues to rise in both income categories (see Figure 3).

Stroke mortality, however, has reduced in low- and middle-income countries (by 20%, 95% CI 15–30), as well as high-income countries (by 37%, 95 % CI 31–41).[12] There is substantial variation between countries, with age-adjusted stroke mortality rates being more than 10-fold higher in the highest ranked country, Russia (251 per 100,000 people) compared with the lowest ranked country, the Seychelles (24 per 100,00 people).[13] A study by Redon and colleagues on stroke mortality in 39 countries from Europe and Central Asia showed the gaps in stroke mortality widened from 1990 to 2006 between western European countries and eastern

European/central Asian countries.[14] A recent study of subarachnoid haemorrhage (SAH) by Guha and colleagues using data from 162 neurosurgical centres in North and Central America, Australia, Europe, and Africa also showed that at higher per-capita GDP was associated with both reduced mortality (at 3 months) and improved neurological outcome.[15]

Ethnicity

Studies of stroke incidence in multi-ethnic populations in both the UK and the USA have highlighted an increased risk of stroke in minority ethnic groups compared to the majority white population.[16–18] In the USA, mortality rates are also higher in minority groups, particularly among black compared to white populations.[19–20] Evidence on the impact of socioeconomic differences between ethnic groups on stroke incidence and mortality is limited; we found only one study, from the US, which addressed this question. This study was a prospective cohort of 2,082 incident strokes, and estimated that 39% of the increased stroke incidence in black Americans compared with non-black Americans was explained by socioeconomic status (estimated by area-based measures).[21] However this estimate had the important limitation of not accounting for conventional risk factors. One study of routine hospital data of young people with stroke in Florida suggested that the 15% excess mortality in black ethnic groups could be explained fully by differences in risk factor profiles, and did not differ by insurance status; but whether this is true more generally is unclear.[18] Whether well-established ethnic differences in stroke incidence and outcome are responsible for some of the apparent SES disparity is still unknown.

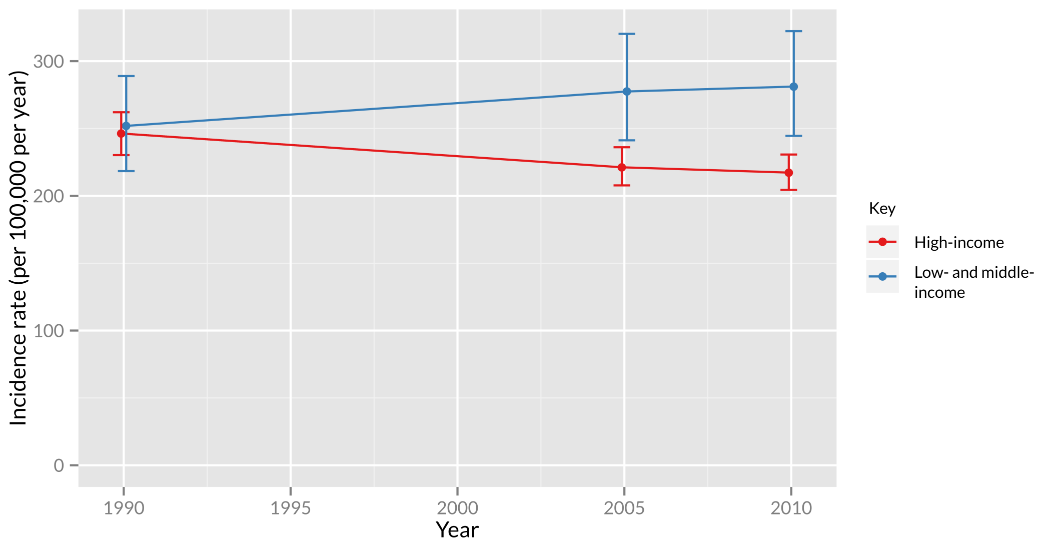

Figure 2: Trends in differences in age-standardised relative stroke incidence between high-income and low- and middle-income countries; data reported in the Global Burden of Disease study by Feigin et al.[12]

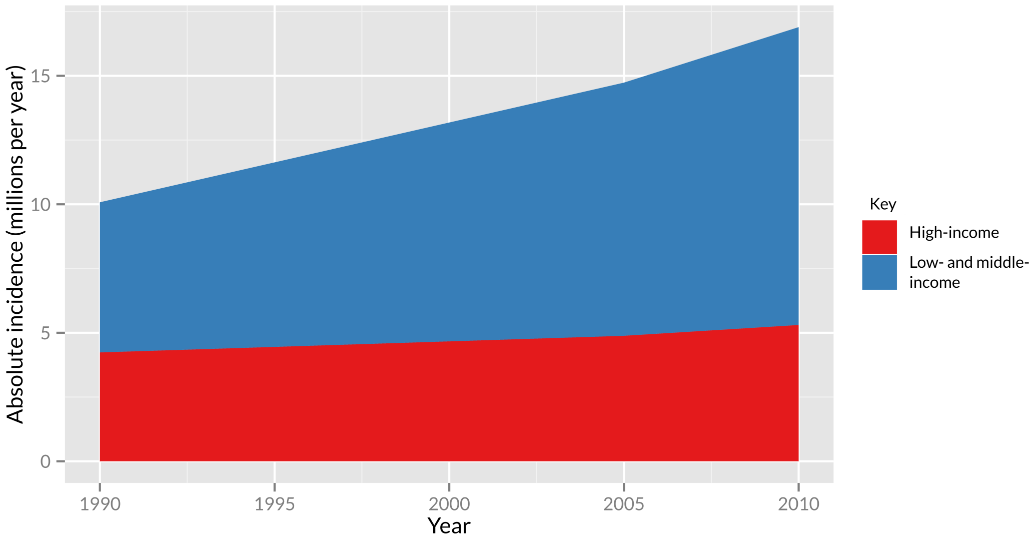

Figure 3: Difference in absolute stroke incidence between high-income and low- and middle-income countries. The relative increase in stroke incidence in low- and middle-income countries is compounded by faster population increase in these countries; data reported in the Global Burden of Disease study by Feigin et al.[12]

Association of SES with stroke incidence

Twenty studies investigating the link between SES and stroke incidence since 2006 are presented in table 2 (see Page 20). Most are high quality population-based studies (17/20 (80%); number of strokes from 177 to 57,690) or studies using linked hospital episode data (3/20 (15%); number of strokes from 6200 to 54,048), but the SES measures used differed widely. Our 2006 review found consistent evidence of an inverse relationship between SES and stroke incidence, albeit mainly from limited lower-quality studies of heterogeneous design.[1]

The new evidence found in this review, especially from high-quality population-based studies with large sample size (n>1000) [2, 9, 10, 21, 23, 29, 84], are generally consistent with the 2006 review. We find that incidence of stroke increases with increasing level of socioeconomic disadvantage, but it differs according to age, sex, and stroke subtype. Several of the studies from table 2 were included in a systematic review (search date 2008), which was able to meta-analyse data from 12 observational studies including an overall population of 171,192 people.[47] This review found high quality evidence that low SES was associated a 67% increased risk of stroke (HR 1.67; 95% CI 1.46–1.91). This analysis did not report the proportions of ischaemic and haemorrhagic stroke.

There are conflicting findings as to whether haemorrhagic stroke is associated with low SES. One Italian hospital-based study (n=2,526 haemorrhages) did find increased haemorrhagic stroke associated with low SES,[22] but no association was found in two population-based Swedish studies [23,24], possibly due to their small sample sizes (n=297 and 47 haemorrhages, respectively). Two English studies[25,26], one nationwide hospital-based (n=6,105 subarachnoid haemorrhage (SAH) admissions in 2010) and one population-based (n=528 SAH), also did not find any association between low SES and SAH.

We found some studies (albeit of lower quality) examining SES in men and women. Three population-based studies in women showed that the risk of stroke is inversely related to the number of years of education completed[24,27,28] though with relatively small sample size (n=200, 451 and 177, respectively). A French study from the population-based Dijon stroke register (n=1433) found that stroke incidence in women was higher in neighbourhoods with greater overall inequality in income, but reported no difference in stroke incidence for men residing in areas with income equality.[29] A population-based Swedish study in men (n=1442) also reported no association between occupation and ischemic or haemorrhagic stroke for younger men (<51 years), but found older men (≥51 years) with unskilled manual occupations had a significantly lower risk of ischemic stroke than high-grade civil servants and executives after controlling for other risk factors (adjusted HR 0.62, 95% CI 0.46 to 0.84).[33] A nationwide cohort study of male civil servants in South Korea (n=785), however, showed that stroke risk was significantly lower in those with highest SES compared with lowest (adjusted HR 0.41, 95% CI 0.32 to 0.54).[87]

In summary, there is high-quality evidence that low SES is generally associated with increasing risk of stroke. The evidence of such association is more consistent in ischemic strokes than in haemorrhagic strokes, and the association might be stronger in women than in men.

Association of SES with stroke outcomes

Mortality

The 2006 review found strong evidence that lower SES was associated with increased stroke mortality, and that this effect was amplified in older age, and in ethnic minorities.[1] Since 2006, large cohort studies, either population or hospital-based, have been published on SES and mortality from several countries, including the US, Canada, the UK and Sweden, which reported similar associations.[4,14,23,34–37]

SES and in-hospital/short-term mortality

A hospital-based study on acute ischemic stroke based on 147,780 hospitalizations in 8 states in the US showed that inpatient mortality was significantly higher for low-income area patients than that for high-income area patients (OR, 1.08; CI: 1.02–1.15) after adjusting for other risk factors.[37] A large nationwide cohort study from the US (n=31,631; US Nationwide Inpatient Sample database 2005–2010) and Canada (n=16,531; Canadian Discharge Abstract Database 2004–2010) of people with SAH found that low income was associated with increased in-hospital mortality in the US (OR for top *v* bottom neighbourhood income quartile: 0.77, 95% CI 0.65 to 0.93 adjusted for demographics, comorbidities, and hospital factors), but not in Canada (OR for top *v* bottom quintile 0.97, 95% CI 0.85 to 1.12).[36] Lai and colleagues' hospital-based study on SAH patients (n=17,559) in the US also showed that Medicare, Medicaid had higher in-hospital mortality compared to those with private insurance (OR for comparison with privately insured: Medicare 1.36, 95% CI 1.16 to 1.58; Medicaid 1.18, 95% CI 1.02 to 1.36; Uninsured 1.09, 95% CI 0.88 to 1.36).[4]

A recent population-based study using a Swedish Stroke Register (Riks-Stroke) of 62,497 patients found that low income, leaving education after primary school, and living alone were independently associated with increased mortality after the acute phase of stroke. Differences in survival related to income and cohabitation appeared early, at 8–28 days after stroke, with the gaps widening thereafter. The association between education and case fatality was not present until 29 days to one-year after stroke. These differences could not be explained by differences in use of secondary prevention treatments.[35] Another population-based Swedish study (n=1648 strokes) also found that low income was associated with higher 28-day and 1-year fatality rates in men, but not in women.[23] A further population-based study (n=806 strokes) in the US[88] using neighbourhood socioeconomic status (NSES) showed mortality at 1 year after stroke was significantly higher among residents with the lowest NSES than those with the highest NSES (HR 1.77, 95% CI: 1.17–2.68) after adjusting for confounding factors. However, a cohort study of 2042 patients admitted to a large teaching

hospital with stroke in Scotland found no association with Carstairs scores (a UK area-level composite SES score) and short term or 12-month mortality, though the those with lower SES had their strokes substantially earlier (mean age 71 for deprived versus 76 for affluent group).[86]
A study of linked hospital and primary care records (37,888 strokes) from Wales from 2004-2011 using the Welsh Index of Multiple Deprivation, found that social deprivation was significantly associated with increase stroke mortality at 30 days and 1 year (30 days mortality, top deprivation quintile v bottom OR: 1.24, 95% CI 1.14 to 1.34, 1 year mortality 1.23, 95% CI 1.15 to 1.33); there was no significant association between SES and SAH mortality.[89] This analysis adjusted for patient demographics and co-morbidities.

SES and long-term mortality

A large Swedish study on 10,487 stroke survivors found that higher socioeconomic position, measured by education and income, was associated with lower mortality at 4 years after stroke, for all-cause mortality and stroke-specific mortality, both overall and with cerebral infarction.[34] However, this result was not adjusted for stroke severity or traditional risk factors such as hypertension and smoking status. In the UK, on the contrary, new data from the population-based South London Stroke Register (n=4398) found no significant difference in long-term survival (up to 17-year follow-up) associated with SES (see figure 4), except in the subgroup of black African and black Caribbean people, and differences associated with ethnic group were not significant once quality indicators of the of acute stroke care were adjusted for.[38]

In summary, there is high-quality evidence that low SES is generally associated with increased risk of in-hospital/short-term mortality but with some inconsistent evidence from contries with universal health care system such as Canda and UK showing no association. The relationship between SES and long-term survival is inconclusive and more high-quality studies on this are needed.

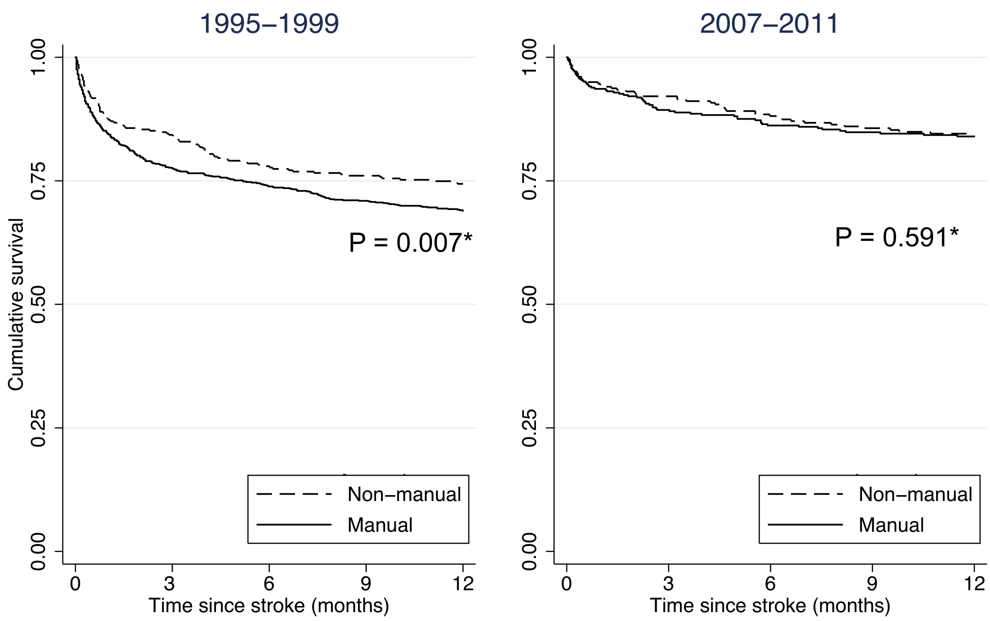

Figure 4: Cumulative survival data by occupational class from the South London Stroke Register, from data published by Chen et al.[38]; *P values presented are adjusted for age, sex, ethnicity, subtype and severity (assessed by incontinence, GCS, dysarthria, dysphasia and failed swallow test); apparent differences in survival between manual and non-manual occupation classification from 1995–99 no longer exist by 2007–11

Stroke severity and functional outcome

The 2006 review found some evidence that low SES was associated with more severe stroke, particularly in patients aged over 65 years.[1] Since 2006 there have been several cohort studies which provided further evidence on the relationship between SES and stroke severity. A prospective cohort study of 1,965 ischemic stroke patients in the US showed that those with lower SES (education, income and employment) had significantly higher odds of post-stroke disability at 3 months (OR of disability: educational attainment of high school or less 1.44, 95% CI 1.12 to 1.85; unemployed v working pre-stroke 3.19, 95% CI 2.02 to 5.02).[39] An analysis of hospital data from 95,986 people with intracerebral haemorrhage in the US between 2003 and 2011 found patients with Medicare or Medicaid were less likely to be independently ambulatory and less likely to be discharged to their own homes than those with private insurance.[40] Similar associations were observed in a population-based German study of 1,688 ischemic stroke patients on relationship between education level and functional impairment (measured using the Barthel index) at 3 months.[41]

A recent study from the population-based South London Stroke Register of 2104 stroke patients showed that socioeconomic deprivation, measured by IMD (Index of Multiple Deprivation), overall was not significantly associated with functional impairment (Barthel index of <15) at 3 months and 3 years after stroke; but did find that lower SES was associated with significantly increased functional impairment for those aged over 65 years, and those with ischemic stroke at any age (ORs for lowest IMD quartile v highest: ≥65 years group OR 1.94, 95% 1.34 to 2.81; ischaemic stroke OR 2.01, 95% CI 1.43 to 2.84).[42] Another analysis of data from the South London Stroke Register found increased post-stroke cognitive impairment in stroke survivors from manual occupational backgrounds compared with non-manual occupations (relative prevalence increase for manual v non-manual: 42%, 95% CI 8 to 86%).[43] A prospective cohort study from the US on cognitive status in 232 subarachnoid haemorrhage (SAH) survivors showed having ≤12 years education significantly increased the chance of cognitive impairment at 1 year after stroke (OR 7.2, P<0.001; 95% CI not reported).[44]

In summary, there is some good-quality evidence that low SES is associated with more severe stroke and poorer functional status at up to one year after stroke. However, evidence on the relationship between SES and long-term functional outcomes is still lacking.

Recurrent stroke

The impact of socioeconomic status on risk of recurrent stroke has been studied less extensively than the impact on first stroke and mortality rates. Three European studies found no overall associations between income level, occupational class or low socioeconomic position and recurrent stroke.[22,23,45] One study conducted in Italy compared rehospitalisation rates for stroke in 10,033 patients initially admitted to hospital with an incident stroke between 2001 and 2004.[22] No association between socioeconomic position and rehospitalisation was found, before or after adjustment for age. In Sweden a population based study of 275 recurrent strokes following 1648 incident strokes also found no associations between the risk of recurrence and income level and occupational class overall.[23] In this study the risk was adjusted for age, marital status, country of birth and housing condition, but not for traditional lifestyle and physiological risk factors. In the UK, the population based South London Stroke Register found no difference in stroke recurrence rates between manual and non-manual occupations in an analysis of 2874 patients, with adjustment for age, gender, ethnicity, stroke subtype, prior-to-stroke risk factors and severity markers of the first stroke.[45]

Although no overall associations were observed in the Swedish or Italian studies, when the data was stratified by gender the Swedish study found an increased risk of recurrence in woman on the lowest incomes but not in men.[23], while the Italian study found low socioeconomic position was associated with an increased risk of ischaemic stroke only in men.[22] As neither of these two studies adjusted traditional risk factors, the apparent gender differences observed may be explained by differences in lifestyle and physiological risk factor profiles.

As neither of these two studies adjusted for stroke risk factors the gender differences observed may be explained by differences in risk factor profiles. At present the evidence on the association, or lack of association, between SES and recurrence is limited. While the three studies above were large and two population based, only one adjusted for risk factors which may account for the differences observed in the two which did not.

Mechanisms of the links between SES and stroke

Traditional risk factors

Disparities in the prevalence of stroke risk factors by socio-economic status, with the highest rates observed in the lowest socioeconomic groups, have been widely reported and were summarised in the 2006 review by Cox et al.[1] An international case-control study of risk factors for stroke across 22 countries compared risk factor prevalence in 3000 cases admitted to hospital with incident strokes to 3000 age and sex matched controls. Traditional risk factors for stroke, namely hypertension, smoking, waist to hip ratio, diet, physical activity level, diabetes and alcohol intake collectively accounted for 88.1% (95% CI 82.3%-92.2%) of the population attributable risk of stroke.[46]

Cox et al. reported that at the time of the 2006 review the extent to which risk factors accounted for differences in stroke incidence and mortality within socio-economic groups was unclear with two Scottish studies suggesting no association between SES and mortality after adjustment, a further UK study finding risk reduced by 50% and a Dutch study finding no reduction after accounting for risk factors.[1] In a 2011 review by Kerr and colleagues, a meta–analysis of 12 studies was conducted to examine the extent to which socio-economic differences in stroke incidence could be attributable to 'traditional' risk factors (used here to refer to hypertension, smoking, diabetes, lipids, atrial fibrillation, existing vascular disease, obesity, and sedentary lifestyle). Once these risk factors were taken into account, the excess stroke risk associated with SES was reduced, but there remained a 31% increase in the hazard of stroke incidence (HR 1.31, (95% CI 1.16–1.48) compared to HR 1.67 (1.16-1.91) without adjustment).[47] The results of this review highlight the need for studies exploring the impact of SES on stroke incidence and outcomes to ensure the effect of risk factors are taken into account in analyses.

Early life influences

A 2006 systematic review by Galobardes et al. highlighted an increased risk of stroke in later life in those from low socioeconomic groups in early childhood using data from 24 prospective, 11 case-control and 5 cross-sectional studies.[48] Other studies have found that this risk remains even after adjustment for socioeconomic position later in life,[1] with adjustment for adult socioeconomic position associated with a one study finding a reduction of only 8% in the risk of stroke associated with low childhood socioeconomic status.[49]

We identified one systematic review (search date 2004) not reported in our previous review, which synthesised data from 49 observational studies examining the associations between childhood adversity and adulthood cardiovascular disease.[55] This review authors concluded there was convincing evidence of a *life-course* model; that is, adverse psychological, physical and environmental risks accumulated over a life-time.

Subsequent large cohort studies have added to this evidence of accumulation of adversities in childhood, with financial difficulties, divorce or bereavements, (which in one study had occurred most commonly in those with lower education levels in adulthood) being associated with increased risk of stroke[53] and overall cardiovascular disease[54] in adulthood even after adjustment for conventional risk factors.

One proposed explanation for the link between SES and stroke is the fetal origins hypothesis, that stroke in adult life is associated with poor nutrition in utero and infancy.[52] Studies included in the 2006 review found associations between reduced intrauterine growth, low birth weight and increased rates of fatal and nonfatal stroke in adult life.[50,51] but we found no further evidence since the last review.

In short, the evidence is strong and consistent of a link between low SES in childhood and adulthood illness. The exact mechanism is still unproven, and increased conventional risk factors among those with lower SES do not explain the full effect.

Quality of health-care provision

Multiple studies have demonstrated that the quality of stroke care, both prevention and treatment, varies substantially both within and between countries; but whether this variation is linked to SES has been less certain. We previously found inconclusive evidence about whether lower SES was associated with lower quality of care.[1] Our 2006 review described studies from Canada[56] and Finland[57] that found that those with low income were less likely to receive high quality in-patient stroke care. However, studies from the UK and the Netherlands found no such association.

More recent evidence from the South London Stroke Register shows that lower SES was associated with reduced odds of hospital admission (of any type) (for quintiles 2—5 combined *v* 1st quintile Carstairs score: OR 0.71, 95% CI 0.54 to 0.94), but no difference in length of stay in a stroke unit, the proportion having CT scans, or proportion having swallowing assessment.[58] The differences in hospital and stroke unit admission due to SES were small, and appeared to be improving over the time assessed (1995–2010). Socioeconomic disparities in care quality were greater in black ethnic groups compared with white ethnicity.[58] Stroke audit data across England (including data on around 70,000 people admitted to hospital with stroke) found wide variation in appropriate brain imaging, but found that it was not explained by deprivation.[59]

In Sweden, using data from 319,240 stroke patients recorded in the nationwide Riks-Stroke register between 1995 and 2009 small significant differences in admission to stroke units were found by level of education (highest educational attainment: secondary OR 1.04, 95% CI 10.1 to 1.07; university OR 1.06, 95% CI 1.01 to 1.10; all versus primary).[60] However, as in London over the same time period, the difference diminished over time as stroke unit capacity increased. Riks-Stroke also reported differences in use of thrombolysis or thromboectomy for people with different levels of education between 2003 and 2009; the lowest rates were in the least educated (secondary education OR 1.18, 95%1.10 to 1.28; university 1.39, 95% CI 1.26 to 1.53; all compared with primary education).[61] When the findings were adjusted for pre-stroke independence, traditional risk factors, stroke severity, and stratified by hospital type it was found that the differences existed only in large non-university hospitals.

Data from 6 European regional and national stroke audits (329,122 patients; Germany, Poland, Scotland, Catalonia, Sweden, and England, Wales, and Northern Ireland) found substantial variation between countries in quality of diagnosis and treatment (brain imaging, stroke unit treatment, thrombolysis, antiplatelet and anticoagulant use, length of stay).[62] However, for most indicators, there was no clear associations found between sociodemographics and use of appropriate treatment.

A study of Danish national-level data from 2003-07 (14,545 people) found low SES associated with reduced odds of having good quality acute treatment (admission to stroke unit; imaging, physiotherapy and occupational therapy assessment, and antiplatelet treatment), and higher early mortality (for low *v* high income groups: good quality acute treatment RR 0.82, 95% CI 0.78 to 0.86; 30-day mortality HR 1.44, 95% CI 1.20 to 1.74).[63] This difference existed whether SES was measured as income, education, or occupation, but the difference in mortality was no longer significant after adjustment for demographics, co-morbidities, and lifestyle risk factors. A similar study in 600 US hospitals (210,212 people with ischaemic stroke) did find substantially reduced use of all imaging modalities in people funded by Medicare and Medicaid (typically comprising older people, those with disabilities, and those on lower income).[64] The difference was smallest with CT scanning, which the authors note is very widely available and done as part of an emergency pathway; large differences were found in use of MRI and non-invasive neck angiography (MRA or CTA) (MRI Head: uninsured 79%, Medicare 64%, Medicaid 74%, private insurance 81% [P<0.001 for each v private] Noninvasive neck angiography: uninsured 30%, Medicare 23%, Medicaid 27%, private insurance 36% [P<0.001 for each v private]).

Two studies from the US (one prospective stroke register, and one retrospective analysis of hospital discharge data) both found that uninsured patients had greater length of stay (3.8 days for uninsured *v* 4.5 days for insured P<0.001 [65]; 8.5 days *v* 6.9 days, significance not reported [66]); the most frequent reason for delay in the first study being lack of access to a rehabilitation unit for the uninsured.[65] A study of subarachnoid haemorrhage using US and Canadian national-level data from 2004–10 found no significant association between being discharged to a rehabilitation units and neighbourhood income differences.[36]

A study of US national data from 2002-10 examined the timeliness of surgical intervention for subarachnoid haemorrhage (78,070 patients having surgical clipping or endovascular coil embolization).[68] It found that those on the Medicaid programme waited longer for their procedure than those with private insurance (OR for waiting >3 days for intervention 1.33 1.15, 1.54). An analysis of the same dataset from 2001-09 of those with unruptured intracranial aneurysms (which may lead to subarachnoid haemorrhage) found that lower SES (estimated as individual income) was associated with lower rates of clipping and coiling (top income quartile v bottom: OR 1.38, 95% CI 1.30 to 1.45).[69]

A further US study of 249,336 nationwide hospital admissions with ischaemic stroke found rates of mechanical thromboectomy were lower in those on Medicare and those uninsured (ORs all compared with those with private insurance: uninsured 0.52, 95% CI 0.25 to 0.95; Medicare 0.53, 95% CI 0.41 to 0.70; Medicaid 1.09, 95% CI 0.70 to 1.65).[70] This difference appears to be due to uninsured patients being substantially less likely to be admitted to hospitals where the procedure is available.

In summary, there is good-quality evidence that low SES is associated with inadequate access to health care; a plausible mechanism by which SES might lead to poor stroke outcomes. However, the impact of health system (universal provision versus private insurance) does not seem to explain this entirely: substantial differences in outcomes remained even in countries with universal health-care provision.

Conclusions and future directions

This paper reviews international epidemiological research on the association between SES and stroke since 2006. The association between socio-economic disadvantage and adverse health, particularly cardiovascular health, has been known for many decades.[71,72] From an international perspective, the evidence is now unequivocal: the international burden of stroke is borne primarily by low- and middle-income countries. These countries, which account for the majority of the world's population, have not benefited from the reduction in stroke incidence and improving outcomes found in high-income countries, and this disparity is increasing over time. This phenomenon can be partly attributed to the success in risk factor identification, treatment, and control in high-income countries;[73,74] this contrasts markedly with poor control rates in low- and middle-income countries.[75,76] Stroke unit care, one of the most clinically effective and cost-effective treatments for acute stroke, are little used in low- and middle- income countries; indeed there remains uncertainty about what stroke unit care in these settings should comprise.[77] Current acute care in much of the developing world is also inconsistent, with large variation in average length of hospital stay and costs between countries.[78]

Within individual countries, a similar, but perhaps more nuanced picture emerges. The increased research attention to SES and stroke in the past 10 years has been remarkable. We note that there have been more relevant studies since the 2006 review than in the entire period before, and many hypothesised associations are now supported by evidence from high quality prospective cohort studies. We summarise several recent large-scale analyses from long-running stroke registers and national audits examining the strength and possible mechanisms of the association between SES and stroke within countries. As in the 2006 review, the vast majority of new study reports found that SES was associated with increased stroke incidence. Low SES has been consistently associated with increased stroke mortality, and there is evidence from the UK and US that stroke survivors with lower SES are likely to have worse stroke outcome, with higher rates disability and cognitive impairment.

There are, however, studies which disagree with this picture, and raise the possibility that SES-related disparities are reducing over time. Four recent large incidence studies, which were not published in time for the review by Kerr and colleagues, found no important differences in stroke incidence due to SES. [26,29,31,32] Reasons for these discrepant results are not clear; it would be appealing to attribute these to reductions in disparity over time (the studies finding no effect of SES are the most recent), or to improvements in health care provision in the countries studied (the UK, France, and Japan). The results from the UK in particular (Figure 4) suggest improvements over time in survival. Indeed, a study of data from 8515 UK general practices found that previous differences in hypertension control had disappeared completely only three years after the introduction of a contract for primary care doctors which included a payment for achieving good blood pressure control for their population.[79] Additionally, a 2013 analysis of the South London Stroke Register found no differences in risk factor profiles prior to stroke or primary prevention use for different socio-economic groups.[80] The possibility remains, however, that idiosyncrasies in the SES measures used, or the particular populations studied in these papers might equally explain the differences.

This update provides stronger evidence of the likely causes of inequalities. The study by Kerr et al. in particular found that nearly half of the excess stroke incidence was attributable to traditional risk factors. [47] It is possible that traditional risk factors in reality account for a greater proportion of the excess risk than is evident from this review; Kaplan and colleagues suggest that conventional study designs would not exclude the possibility of traditional risk factors explaining SES-related differences fully.[81] Those in lower socioeconomic groups are more likely to be exposed to multiple risks, and risk factors in combination have been postulated to have a multiplicative effect.[82] If this is the case, analyses which adjust for risk factors individually would underestimate their importance. Increasing research demonstrating the association of childhood SES with stroke risk suggests that stroke prevention needs to go beyond adult risk reduction, targeting issues such as childhood nutrition and obesity.

Several key unanswered questions remain. The interaction between ethnicity and SES remains unclear, and there is a need for research into whether well-established ethnic disparities in stroke incidence and outcome explain some of the effect of SES (or vice versa). Internationally, studies have differed on whether people with lower SES have less good quality health care. The variation in care quality found in the US studies is perhaps not surprising, since these studies analysed by insurance status. However, several studies in countries with universal, state-provided health care including Canada, Finland, and Denmark using other SES measures found a similar variation. Whether there are characteristics of the health systems in the UK, Poland, Germany, and Spain (where studies found no SES-related variation) which have successfully reduced inequality, or whether these are artefacts of heterogeneous populations, study designs, or the SES measures used remains unclear. Developing standardised metrics for SES which can be compared between countries is a major challenge, but achieving this may help understand the mechanisms by which SES operates, and illuminate successful strategies and interventions for reducing health disparities. Incorporating both national-level and individual-level data on income, occupation, and education into a single metric may provide a route to achieving this.

For future research, the problem of stroke in low- and middle-income countries is key. Priorities include how to achieve the full potential of risk factor reduction in different settings through public health programmes and improved primary care, and improving the quality and consistency of acute hospital care. For socio-economic disparities within countries, efforts to control traditional risk factors in lower SES populations together with ensuring equity of access to high-quality acute hospital care and rehabilitation remain crucial. Recent research offers a glimmer of hope that these strategies are beginning to show effect.

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Contributors

IJM, YW, SC, and CDAW designed and produced the review outline with input from all authors, IJM conducted the search, IJM, YW, and SC assessed articles for inclusion, IJM, YW, and SC produced the initial draft the manuscript and figures, all authors critically revised multiple drafts, and approved the final version.

Declarations of interests

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Table 2 - Studies on SES and stroke incidence published since 2006

Study	Location	Design	Participants (n)	Time span	Age (years)	Measures of SES	Relevant findings
Avendano et al, 2006[83]	New Haven, Conneticut, United States	Population-based cohort study of older population (aged 65 and over)	2812 people, 270 strokes	1982–94	≥65 at baseline	Education and income	For those aged 65–74, low education (HR 2.07, 95% CI, 1.04 to 4.13) and low income (HR 2.08, 95% CI, 1.01 to 4.27) were associated with increased stroke risk
Avendano et al, 2008[84]	United States	Population-based cohort study of population aged over 50 (those with stroke at baseline not included)	22,672 people, 1542 strokes	1992–2004	≥50 at baseline	Education	Low wealth, and low income both associated with increased stroke risk (adjusted hazard ratios for stroke with wealth, bottom decile v 75–95th percentile: 2.3 (95% CI 1.6 to 3.4), and for income: 1.8 (95% CI 1.3 to 2.6)
Grimaud et al, 2011[29]	Dijon, France	Population-based stroke register	62,299 residents; 1433 strokes	1995-2003	≥40	Area-level socioeconomic indicators	Among women, stroke incidence was higher in neighbourhoods with large income inequality (incidence rate ratio (IRR), 1.34; P=0.003); Among men, no associations between SES and stroke incidence overall, except for age group between 40 and 59 years (IRR, 1.56, P=0.01).
Heeley et al, 2011 [10]	3 studies pooled: a) Perth, Australia; b) Melbourne, Australia; c) Auckland, New Zealand.	Population-based studies. Data was pooled from three population-based stroke registers with similar methods; (the Melbourne study was reported separately by Thrift et al.)	1,741,765 person-years assessed; 3133 strokes	a) 1995–96 and 2000–01 b) 1996–99 c) 2002–03	Mean age 73 years, SD 14	Australian Index of Relative Socioeconomic Disadvantage (IRSD); New Zealand index of deprivation (NZDep)	Stroke incidence rates were significantly and substantially higher among the most deprived quintile versus the least deprived quintile (Incidence rates 131 per 100,000 person-years for least deprived v 71 per 100,000 person-years for most deprived; IRR 1.70, 95% CI 1.47 to 1.95)

Honjo et al, 2008[27]	Japan	Population-based prospective study	20,543 women, 451 strokes	1990-2002	40-59	Education level, employment status and social role in the household	Women with junior high school education showed a higher incidence of total stroke, subarachnoid hemorrhage, and ischemic stroke compared to high school graduates.
Honjo et al, 2010[31]	Japan	Population-based prospective cohort study	10,640 residents; 197 male strokes; 170 female strokes	1992-2005	≥20	Education level and occupation	No significant associations between education level and/or occupation and risk of total stroke, subarachnoid hemorrhage, or ischemic stroke for men, and for women (except subarachnoid hemorrhage).
Honjo et al, 2015[32]	Japan	Population-based study (Public health centre based prospective study)	90,843 participants; 4410 strokes.	1990-2010	40-69	Small area deprivation index consisting of a weighted sum of deprivation-related census-based variables.	Neighbourhood deprivation level influences stroke incidence in Japan, which becomes non-significant after adjusting for CVD risk factors.
Jackson et al, 2014[28]	Australia	Population-based study of women (national)	11,468 women; 177 strokes during a 12-year follow-up.	1996-2010	47-52	Education, occupation and homeownership.	Lower education level and non-homeownership (but not occupation) are associated with increased stroke risk in mid-aged women, partially mediated by known risk factors
Kleindorfer et al, 2006[21]	Greater Cincinnati, United States	Population-based stroke register	1.35 million residents; 2082 strokes	1999	Mean age 70.3 years, SD 15.5	Community SES measures including poverty, education, crowding, and median household income	Poorer community SES was significantly associated with higher stroke incidence (p=0.003) and may explain some of the racial disparity in stroke incidence.
Kuper et al, 2007[24]	Sweden	Population-based record linkage cohort study	47,942 women; 200 strokes	1991-2002	30-50 at baseline	Education level	Risk of stroke inversely related to years of education completed (comparing lowest with highest education group, HR=1.5; CI: 1.0 to 2.2 after adjustment for established risk factors. The gradient was more pronounced for ischemic stroke (2.9,

							CI: 1.8 to 4.7) than for hemorrhagic stroke (1.4, CI: 0.7 to 2.9).
Li et al, 2008[23]	Malmo, Sweden	Population-based record linkage with national population registers and the stroke register in Malmo	69,625 residents; 1648 strokes	1990-2001	40-65 at baseline	Total annual income and occupation class	Incidence of stroke increased with decreasing socioeconomic status (by income) in women (RR: 1.75, 95% CI: 1.36 to 2.25) and in men (RR 1.29, 95% CI 1.06 to 1.58). Low income was significantly associated with ischemic, but not hemorrhagic. Similar relationships were found between occupation level and incidence of stroke.
McFadden et al, 2009[85]	Norfolk, UK	Population-based prospective cohort study	22,488 people, 683 strokes	Recruited 1993–97, follow up until 2007	39–79	Occupational social class (Registrar General's occupation-based classification)	Stroke incidence was substantially higher in social class V v class I; this difference was similar after adjusting for blood pressure, cholesterol, diabetes, smoking, and body mass index (unadjusted HR 2.62, 95% CI 1.63 to 4.22; adjusted HR 2.55, 95% CI 1.34 to 4.85
Novak et al, 2013[33]	Gothenburg, Sweden	Population-based cohort study	6994 men; 1442 strokes over a 35-year period.	1970-2008	47–56	Occupation	Overall, occupational class was not associated with either ischemic or hemorrhagic stroke. However, older men (≥51 years at baseline) with unskilled manual occupations had a significantly lower risk of ischemic stroke than those high-grade civil servants and executives, even after controlling for other risk factors and competing risks of death. No association between occupation and stroke of either type was detected for men younger than 51 years.

Pujades-Rodriguez et al, 2014[26]	England	Population-based record linkage cohort study	1.93 million patients; TIA, n=4412; Ischemic strokes, n=2314; intracerebral haemorrhage, n=892; subarachnoid haemorrhage, =528	1997-2010	≥ 30	Index of multiple deprivation (IMD) - a small-area socioeconomic deprivation indicator commonly used in the UK.	No association was observed with subarachnoid haemorrhage and transient ischaemic attack. Lifetime risk difference between least and most deprived quintiles was small or negligible for transient ischaemic attack, ischaemic and intracerebral haemorrhage, in both women and men.
Seo et al, 2014[3]	South Korea	Population-based study	21.77 million residents; 57 690 strokes	2005	All ages	Income and medical insurance	Incidence of stroke increases as the income level decreases, but it differs according to sex, age, and stroke subtype.
Thrift et al, 2006[9]	Melbourne, Australia	Population-based stroke register (also included in pooled data by Heeley et al.)	306,631 residents; 1421 strokes	1997-1999	45-84	Australian Index of Relative Socioeconomic Disadvantage (IRSD)	Fatal and nonfatal stroke incidence increased with increasing level of socioeconomic disadvantage.
Andersen et al, 2014[30]	Denmark	Hospital-based study (national)	Denmark population (≥40 years old); 54,048 strokes.	2003-2012	≥40	Education and income	Risk for hospitalization for a first ischemic stroke was nearly doubled for people in the lowest income group; there was a 36% increased risk for those with the shortest education (those<65 years). Smoking, obesity, alcohol consumption, and diabetes seem associated with people with lower socioeconomic position.
Cesaroni et al, 2009[22]	Rome, Italy	Hospital-based data (regional)	2.7 million residents; 10,033 strokes	2001-2004	35-84	Small-area composite index	Low SES groups had higher rates of ischaemic (RR: 1.72 to 1.76, all $p<0.05$) and hemorrhagic (RR: 1.37 to 1.50, all $p<0.05$)
Shiue, 2013[25]	England	Hospital-based data (national)	England population: 53 million (2011); 6105 SAH admissions in 2010	2008-2011	40-80	The English Indices of Deprivation, including Index of Multiple Deprivation scores.	Areas with higher prevalence of risk contributors had higher SAH admissions (all $p < 0.05$), but no relation with deprivation was found.

Song et al, 2006[87]	South Korea	Cohort study of male civil servants (national)	578,756 men, 785 strokes	1990-2001	30–58	Monthly salary, grouped into quartiles	Stroke hazard was significantly lower in those with highest SES compared with lowest (adjusted HR 0.41, 95% CI 0.32 to 0.54)